PRINCIPAL INVESTIGATOR: Mark Roschewski, M.D.

STUDY TITLE: A Phase 1 Study of Venetoclax added to Magrolimab and Obinutuzumab for Relapsed and Refractory Indolent B-cell Malignancies

STUDY SITE: NIH Clinical Center

Cohort: Affected patient

Consent Version: 12/08/2023

WHO DO YOU CONTACT ABOUT THIS STUDY?

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KEY INFORMATION ABOUT THIS RESEARCH

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). This section provides the information we believe is most helpful and important to you in making your decision about participating in this study. Additional information that may help you decide can be found in other sections of the document. Taking part in research at the NIH is your choice.

You are being asked to take part in this study because you have an indolent B-cell lymphoma and your disease has returned or progressed after other treatment. You have completed screening for this study and the test results show that you are able to take part in this treatment part of the study.

The main purpose of this study is to find out if it is safe to give the combination of three drugs – magrolimab, obinutuzumab, venetoclax – to patients with B-cell lymphomas. Specifically, we will look at patients with follicular lymphoma (FL), marginal zone lymphoma (MZL), mantle cell lymphoma (MCL) and chronic lymphocytic leukemia (CLL).

Although obinutuzumab (GAZYVA®) and venetoclax (VENCLEXTA™) have been approved and used either alone or in combination to treat types of lymphoma, magrolimab has not. **The use of magrolimab in this research study is experimental, which means that the FDA has not approved its use for cancer treatment or treatment of any other disease**. In addition, **the combination of magrolimab, obinutuzumab, venetoclax in this study is experimental**, which means that while the FDA has approved obinutuzumab and venetoclax for cancer treatment, they have not approved the combination of obinutuzumab and venetoclax with magrolimab.

We want to study the side effects of these drugs when given together. We also want to see if the combination of these three drugs is an effective treatment for your disease, and hope to learn about how they work together to treat B-cell lymphomas.

There are other drugs and treatments that may be used for your disease, and these can be prescribed by your regular cancer doctor, should you decide to not be on this study. If you would prefer other drugs or treatments, you should consider not joining this study. The side effects of other treatments may be similar to those that you might have in this study.

If you decide to join this study, here are some of the most important things that you should know that will happen:

- Treatment will last for about 8 months and will require you to come in for check-ups about every 4 weeks. You will be assigned to an experimental treatment group based on your specific type of lymphoma.
- In the first part of the study (dose finding phase), we want to find the highest dose of venetoclax that is safe to use with magrolimab and obinutuzumab. We will test the highest dose of venetoclax in small groups of patients and see what side effects the combination of these medications might cause. We will decrease the dose of venetoclax in the next small group of patients if needed. After the first part is done, we will enroll additional patients in a second part of the study (dose expansion phase) to learn more about whether these study medications can effectively treat your cancer.
- If you are part of the dose-finding phase of the study, and are tolerating the combination of drugs well, you will receive 6 cycles of treatment, 28-days each (except for the first cycle for MZL, MCL and CLL participants which will be 35 days). After that, you may be able to receive more cycles of treatments if your cancer is responding well.
- If you are part of the dose expansion phase of the study, you will receive 8 cycles of treatment- the first 2 cycles (28-days each) with magrolimab and obinutuzumab alone ("window" period), and the next 6 cycles of all three study drugs together (triplet combination therapy), each cycle lasting 28 days (except for the first cycle of the triplet combination for MZL, MCL and CLL participants, which will be 35 days). After that, you may be able to receive more cycles of treatments if your cancer is responding well.
- You may have side effects from the treatment. Some can be mild or very serious, temporary, long-lasting, or permanent, and may include death. Examples of some of the side effects that you may have include: changes in blood counts (such as low red or white cells), gastrointestinal (such diarrhea, nausea, vomiting), fatigue, bleeding and bruising, rash, and infections. Some side effects may affect your ability to have children. You may also have side effects from some of the procedures (such as lymph node biopsies) and bone marrow tests. All of the possible side effects are described in more detail later in the consent form.
- You will be seen regularly during the study. You will have clinical, laboratory, and imaging tests to see how you are doing and to assess your disease. We will also collect required samples from you (including blood, bone marrow, and tumor biopsies) for both clinical and research purposes. We may also collect saliva or cheek swabs for research that involves genetic testing to better understand the disease and how it responds to the drug.

- After the study treatment has ended, we will need to see you about 30 days after the last dose of study drugs at the NIH Clinical Center. We will continue to see you about every 3-6 months for about 5 years after treatment, and then at least yearly to see how you are doing and if your cancer gets worse (or comes back). After this time, we may contact you to see how you are doing for the rest of your life or until the study ends.

Just as we do not know what side-effects you might have; we cannot know if you may benefit from taking part in this study. If you do not benefit, this study and the results from our research will help others in the future.

You are free to stop participating in the trial at any time. If you decide to stop, the study doctor may ask you to agree to certain tests to make sure it is safe for you to stop.

The remaining document will now describe the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with you about the information in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time you need to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

B-cell lymphoma is a cancer of certain white blood cells (called lymphocytes) that are found in lymph nodes and the cancer affects the lymphatic system. The lymphatic system helps to fight infections and disease. The purpose of this research study is to see if the combination of magrolimab, obinutuzumab, and venetoclax is safe and effective at treating different types of B-cell lymphoma. We are asking you to join this research study because you have either follicular lymphoma (FL), marginal zone lymphoma (MZL), mantle cell lymphoma (MCL) or chronic lymphocytic leukemia (CLL) and your disease has returned or progressed. You have already taken part in the screening portion of this study and are able to participate.

Additional information is provided about each of the drugs being combined for the purposes of this study:

- Venetoclax (VENCLEXTA™) is a drug that targets a specific protein in the body called BCL-2. When normal cells are damaged or old, your body tells them to self-destruct. This natural process is called apoptosis. In some lymphomas, BCL-2 may build up and prevent cancer cells from self-destructing naturally. By targeting BCL-2 with venetoclax, the process of apoptosis may be restored, allowing your body to destroy cancer cells.
- Obinutuzumab (GAZYVA®) is a type of drug called a "monoclonal antibody". It is believed that obinutuzumab works by targeting a specific protein in the body called CD20.

CD20 is found on the surface of B-cells in the body, often in high amounts in some types of lymphoma. By using obinutuzumab to target CD20 and attach to it, it may work by causing the cell to die or by signaling your immune system to destroy the cancer cells.

- Magrolimab is also a "monoclonal antibody". It is believed that magrolimab works by targeting a specific protein in the body called CD47. CD47 is a protein on the surface of cancer cell that sends a "do not eat me" signal to the body's immune system. Blocking this protein with an anti-CD47 antibody such as magrolimab may allow the body's immune system to recognize and kill these cancer cells.

Although obinutuzumab (GAZYVA®) and venetoclax (VENCLEXTA™) have been approved and used either alone or in combination to treat types of lymphoma, magrolimab has not. **The use of magrolimab in this research study is experimental, which means that the FDA has not approved its use for cancer treatment or treatment of any other disease**. In addition, **the combination of magrolimab, obinutuzumab, venetoclax in this study is experimental**, which means that while the FDA has approved obinutuzumab and venetoclax for cancer treatment, they have not approved the combination of obinutuzumab and venetoclax with magrolimab. However, the FDA has given us permission to use these drugs together in this study.

We want to study the side effects of these drugs when given together. We also want to see if the combination of these drugs is effective treatment for your disease and hope to learn about how these drug work together to treat B-cell lymphomas.

WHAT WILL HAPPEN DURING THE STUDY?

Study Treatment

The screening process showed that you are eligible to participate in the study, and if you choose to be in it, you may need to have a few additional standard tests completed if not done recently. You will also have additional samples collected for research tests. You may then begin treatment on the study. You will be seen in the clinic at least every 4 weeks while on the study, with more frequent scheduled visits during some cycles. This is described in detail below.

You will be assigned to a treatment arm depending on your specific type of lymphoma. The study has two parts in terms of patient enrollment, and your length of treatment will depend on how well you are tolerating the treatment, what part of the study you are in, and how well your disease is responding to treatment**.**

You will receive "cycles" of treatment; each cycle is around 4 weeks (28 days) – see exceptions below. The treatment is expected to last at least 6 dosing cycles if you are in the dose-finding phase of the study (1 cycle of venetoclax dose-finding together with magrolimab and obinutuzumab, and another 5 cycles of the triplet combination after that) but may continue for up to 12 dosing cycles. If you are part of the dose expansion phase treatment is expected to last at least 8 dosing cycles (2 cycles of obinutuzumab and magrolimab alone [Window period], and another 6 cycles of the triplet combination after that) but may continue for up to 14 dosing cycles.

Dose-finding phase: We do this portion of the study because we want to find the safe dose of venetoclax, when given together with magrolimab and obinutuzumab. First a group of 6 patients will receive venetoclax at the highest dose with magrolimab and obinutuzumab. All patients will receive the same doses of magrolimab and obinutuzumab. This group of patients will be watched

for serious side effects from the combination of venetoclax, magrolimab and obinutuzumab during the first cycle. The first cycle for patients with FL will be 28 days long, with venetoclax given at the desired dose. The first cycle for patients with MCL, MZL and CLL will be 35 days long with venetoclax given in a "ramp-up" schedule- which means that these patients will start venetoclax at a lower dose and have the dose gradually increased every week until the desired dose is reached. If no serious side effects are found, all future patients will receive that dose of venetoclax . If however, there are serious side effects, the dose of venetoclax will be lowered in the next group of 6 patients.

If tolerated, patients will continue on to receive 5 more cycles of magrolimab, obinutuzumab and venetoclax (28-days cycles), meaning they will receive 6 cycles in total. An additional 6 cycles of treatment will be available if patients do not achieve a complete response to treatment and the investigator thinks it is in the best interest of the patient.

Dose expansion phase: Once the safe dose of venetoclax, when given together with magrolimab and obinutuzumab, is determined, then the next part of the study will begin. In this part of the study, patients will receive the safest dose of venetoclax, as determined in the dose-finding phase, together with the same doses of magrolimab and obinutuzumab to learn more about effectiveness of the triplet drug combination in treating B-cell lymphoma.

Patients enrolled onto the **Expansion phase** of the study will receive treatment as follows:

- **Window period:** For the first 2 cycles (Cycle -1 and -2, 28-days each), obinutuzumab and magrolimab will be given without venetoclax to see the early clinical activity and response to these drugs alone.
- **Triplet combination therapy period:** After completing the window, venetoclax will be added at the dose determined in the dose-finding phase of the study. During Cycle 1 of triplet combination therapy, patients with FL will receive venetoclax at the target dose for a 28-day cycle. Patients with MZL, MCL and CLL will be given venetoclax in a "ramp-up" schedule as described above for Cycle 1 (35-days long), which means venetoclax will start at a lower dose and doses will be increased weekly to attain a desired dose during the first cycle of triplet combination therapy.

After completion of Cycle 1, all patients in the dose-expansion phase will be treated with an additional 5, 28-day- cycles of venetoclax, magrolimab and obinutuzumab. An additional 6 cycles (i.e., 14 cycles total) of treatment will be available to patients whose disease is stable or if they do not achieve a complete response to treatment and they relapse and the investigator thinks it is in the best interest of the patient.

The treatment drugs and schedule for each study drug is described in more detail here:

- Venetoclax: This is an oral drug, taken by mouth daily on Days 1-28 or Day 1-35 of every cycle, except for the first 2 cycles of the Window Period for patients in dose-expansion phase of the study. Do not break or chew the tablets. Venetoclax tablets should be taken with a glass of water and should be taken with food. You will receive a supply of venetoclax to take at home on the days you are not seen in the clinic. You should take the tablets at about the same time each day. If you do not remember to take all or any of the medications, do not make-up the dose or take extra the following day to make-up for the missed dose.

You should store the medicine at room temperature . You will be given a drug diary to help you remember the schedule and to record each dose that you take, if you choose to do so. We will ask you to bring this diary and any leftover supply of study medications to each clinic visit.

When venetoclax is started in patients with MZL, MCL and CLL (Cycle 1) it will be given in a "ramp-up" schedule as mentioned above. Starting with the second cycle that of venetoclax, you will take the same dose each day. The study staff will review the doses and schedule with you. Venetoclax will be given from the start at a fixed dose in patients with FL without safety ramp-up.

- Obinutuzumab: Obinutuzumab will be administered by intravenous (IV) infusion for about 4 hours on Days 1, 2, 8, and 15 of the first cycle for all patients (Cycle 1 for patients in the dose-finding phase of the study, and Cycle -2 of the Window: Period for patients in the dose-expansion phase of the study. Obinutuzumab will be administered by intravenous (IV) infusion for about 4 hours on Day 1 of all subsequent cycles. Before each infusion you will receive premedications to help lessen or prevent some side effects. On days when obinutuzumab and magrolimab are administered on the same day, obinutuzumab will be administered approximately 1 hour after magrolimab.
- Magrolimab: Magrolimab will be administered by IV infusion on Days 2, 8, 15 and 22 on of the first cycle for all patients (Cycle 1 for patients in the dose-finding phase of the study, and Cycle -2 of the Window: Period for patients in the dose-expansion phase of the study. After that, magrolimab will be administered on Days 1 and 15 of all subsequent cycles. Your first infusion of magrolimab will take approximately 3 hours. After that all infusions will take approximately 2 hours. Before the first two infusions, you will receive premedications to help lessen or prevent some side effects. We will check your complete blood count (CBC) within 6 hours of the first and second dose of magrolimib (Cycle 1 on Days 2 and 8 for patients in the dose-finding phase of the study; and Cycle -2 on Days 2 and 8 for patients in the dose-expansion phase of the study). We will also check the CBC twice weekly for the first cycle during both the dose-finding and dose-expansion phases of the study.

Additional Information

During the study, you may not receive any live vaccines, and may need to avoid certain medications. Examples of live vaccines include but are not limited to: the intranasal influenza vaccine known as Flu-Mist, measles, mumps, rubella, varicella/zoster, yellow fever, rabies, BCG, and typhoid vaccine Before, you start taking any new medicines, including medicines you can buy 'over-the-counter', please talk to the study doctor to make sure they are allowed on this study.

In addition, avoid eating grapefruit, Seville oranges (bitter oranges) and star fruit while on this study as they interfere with venetoclax. Please be aware that these fruits can be processed into preserves (e.g., marmalade), juice drinks and food supplements; these should also be avoided.

Assessments during treatment

Similar to the tests done at the beginning of the study, many of the same tests will be repeated during the study to see how you are doing and how the cancer may be responding to treatment.

Some of these tests may be performed more often if felt to be needed clinically for your care by your doctor:

Before starting treatment and before the start of every cycle and at the end of treatment or when your disease progresses:

- Review of medical history, and a physical exam (check weight and vitals), including obtaining information about how you function in your daily activities, side effects and symptoms, and review of medications
- Routine blood and urine tests (Approximately 2.9 tablespoons will be collected at each timepoint):
    - Tests to measure your blood counts and organ function (such as liver and kidneys), and blood electrolytes.
    - Tests to measure how well your blood clots
    - If you are a woman able to get pregnant and you are not already known to be pregnant, you will also have a pregnancy test done (this may be done by blood or urine test)
    - Tests routinely done in patients with your type of cancer to confirm the status of your disease

At the time of disease evaluation:

- Bone marrow testing will be repeated if the previous test result was positive to confirm response to treatment.
- Imaging to show all sites of disease, including CT and/or MRI scans (if your doctor thinks they are necessary), and PET scans .
    - CT and/or MRI scans will be done before starting treatment, at the end of the Window period (dose expansion patients only) or before Cycle 1, and then every 3 cycles (after Cycle 3, 6, 9 and 12 -if you have that many cycles of treatment).
    - PET scans will be done before starting treatment, at the end of the Window period (dose expansion patients only) or before Cycle 1, and then every 6 cycles (after Cycle 6 and 12- if you have that many cycles of treatment).

Additional research testing

In addition to the tests that we will conduct to determine whether you are having side effects or if you are responding to the study therapy, we will also collect samples from you for purposes of research only. The samples are being done to look at the effects of therapy on your immune system and markers of tumor activity, including collecting and testing tumor cells. We will also collect samples to perform genetic analysis on your tumor tissue, to determine which genes are expressed both before and after treatment. Gene expression is when the information stored in our DNA is converted into instructions for making proteins or other molecules. This process allows a cell to respond to its environment. We are interested to know if the study therapy changes the environment around the tumor.

Research samples for this study include the following. These samples are required unless otherwise noted:

- Blood Samples for Research: Samples will be drawn to learn more about how the study drugs affect your body, and your cancer, blood samples will be collected on Days 1, 8 and 15 of the first cycle of the Window period and after the first and second cycles of the Window period (for patients in the dose expansion phase), and for all patients after Cycles 3,6,9, and 12, and once you are finished treatment in follow-up (see below). Approximately 2.7 tablespoons will be collected at each timepoint.
- Blood Samples for Pharmacokinetics (PK) and Anti-Drug Antibody (ADA): To check how much of the drug magrolimab is in your blood and the presence of anti-magrolimab antibodies, blood samples will be collected on Day 1 of the first Cycle of the Window period and Day 1 of Cycles 1, 3, 7 and 11 for patients in the dose expansion phase, and on Day 1 of Cycles 1, 3 , 5 and 9 and after Cycle 12 for patients in the dose-finding phase. Approximately 0.5 tablespoons will be collected at each timepoint.
- Bone Marrow Samples: These will be done before starting treatment, during the first cycle of the Window period (optional-only for those patients in the dose expansion phase), at the time of response (improvement or progression), and after 6 cycles of triplet combination treatment. Any bone marrow samples will be collected in the same way as those routinely done to monitor your disease and we will try to collect at the same time, whenever possible.
- Cheek Swab or Saliva Samples: A required cheek swab and/or saliva sample to collect normal tissue will be done, before starting treatment. To obtain a cheek swab, a small brush is rubbed against the inside of the cheek to wipe off some cells. To obtain saliva, a special collection tube will be used and it may take a few minutes to collect the saliva.
- Tumor Tissue and Biopsies: A portion of the biopsies done in the past for your cancer will be collected and are required. We will ask you to undergo a tumor biopsy before starting treatment (if there is not enough tissue from prior biopsies for research), and during Cycle 1 of the Window period (optional-only for patients in the dose expansion phase), and if your disease should progress/ at the end of treatment, only if it is safe to do so. The biopsies are being collected for special research tests. Your decision if to have the biopsies will be documented in the medical record. You may agree to biopsies now and change your mind later. If at any time you do not want to have a biopsy done, please tell us.

  Usually tissue can be obtained safely and comfortably with local anesthesia. However, in some cases, we may need to use conscious sedation which is usually given during minor surgical procedures to relax participants and minimize discomfort. It can be given as a pill, a shot, an IV or even inhaled. You may have to wait up to an hour to start feel the effects depending on how it is given. Once it takes effect, you will be mostly awake, though relaxed or drowsy. You will be monitored throughout the procedure for any changes to your breathing and blood pressure. If you require conscious sedation before undergoing a biopsy, you will be informed of the risks and you will be asked to sign an additional consent prior to undergoing the procedure. Biopsies will NOT be done on this study if they require general anesthesia. We may ask that you have ultrasound or CT scan to help clearly locate your tumor when doing a biopsy.

All of your samples collected for research purposes on this study (such as the tumor and normal tissue) may be used to look for specific changes in the DNA in tumors that could be used to develop new ways of diagnosing and treating cancer. DNA (also called deoxyribonucleic acid) in the cells

carries genetic information and passes it from one generation of cells to the next – like an instruction manual. Normal tissue contains the DNA (instructions) that you were born with, DNA in tumor cells has changed – or mutated – and we think that change in the DNA is what causes tumors to form and to grow.

To look at your DNA, we may use do what is called "whole genome sequencing." This where we will do special tests in the lab to look at the entire sequence, or order, of how your DNA is put together. This is what makes you unique.

To determine which parts of the DNA have mutated, we will compare the DNA in your tumor cells to DNA from your normal cells. We will then analyze the results from similar tumors to see if there are any changes in the DNA that are common to a particular type of tumor. To examine the tumor and normal tissue we may use several different techniques depending on the type of tissue we collect. These could include growing cell lines (cells which keep dividing and growing in the laboratory, sometimes for years allowing us to continually study those cells), xenograft studies (placing or growing cells in another animal, such as mice), and looking in detail at the parts of the genes that produce specific proteins.

However, you should know that the analyses that we perform in our laboratory are for research purposes only; they are not nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing or testing for routine clinical care. For these reasons, we will not give you the results of the research tests done on your research samples in most cases. There may be exceptions to what we share with you and this is described later in this consent form in the section for "Return of research results."

When you are finished taking the drugs (treatment)

When you are finished the study treatment, we will ask you to come to the clinic for follow-up visits and assessments at about the following times: about 30 days after the last treatment, every 3 months for the first 2 years, every 6 months for the next 3 years, and then about yearly after that for as long as your doctor thinks it is necessary or beneficial, unless your disease comes back (or worsens) or you need other treatment not in this study.

These clinic visits will include having physical exams, routine laboratory tests and other procedures, as needed, to see how you are doing, and may also include imaging to check the status of your cancer. At most of these visits, research blood samples will also be collected. If at any time your disease comes back or worsens, we will ask to collect blood and tissue samples (biopsy) for the study.

If your disease worsens, or you need to start a new anti-cancer treatment not in this study, we will continue to follow-up with you by phone every 3-6 months to see how you are doing, for the rest of your life.

HOW LONG WILL THE STUDY TAKE?

If you agree to take part in this study, your involvement is expected to last for the rest of your life.

You will be seen several times during treatment (at least 10 visits) and then in follow-up every 3-6 months for about 5 years after treatment (about 14 visits). During follow-up after the treatment, the number of visits will depend on how you are doing and if your cancer gets worse. The

outpatient visits during and after treatment usually take about 3 hours but should not take longer than 8 hours.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

We plan to have approximately 76 people participate in this study at the NIH.

WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE STUDY?

You should talk to your study doctor about any symptoms that you experience while taking part in the study.

What side effects or risks can I expect from being in this study?

If you choose to take part in this study, there is a risk that:

- you may lose time at work or home and spend more time in the hospital or doctor's office than usual
- you may also be asked sensitive or private questions which you normally do not discuss

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.
- The study doctor will provide you with information about other drugs you may need to avoid while receiving the study drug.

The tables below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

You should report and discuss with the study doctor any other medication(s) you are taking while you are treated with the study drug, so that he/she can take action to prevent any potential drug interactions.

Risks from the study drugs

Venetoclax (VENCLEXTA™)

Likely:

- Low white blood cell count (cells that help fight infection) (neutropenia)
- Low red blood cell count (anemia)
- Low platelet count (cells that help blood to clot) (thrombocytopenia)
- Diarrhea
- Nausea
- Fatigue (feeling tired)
- Upper respiratory tract infection

Less Likely:

- Low white blood cell counts with fever (febrile neutropenia)
- Vomiting
- Constipation
- Fever (pyrexia)
- Swelling of the hands and feet (peripheral edema)
- Pneumonia
- Chemical imbalance in blood (including low potassium, high potassium, high phosphate, high levels of uric acid, lactate dehydrogenase)
- Back pain
- Headache
- Cough
- Dizziness (syncope)
- Infection (including lower respiratory infection and urinary tract infection)
- Low levels of oxygen in the blood (hypoxia)

Rare but Serious:

- Unusual levels of chemicals in the blood caused by the fast breakdown of cancer cells, which may lead to changes in kidney function, abnormal heartbeat, or seizures (Tumor Lysis Syndrome)
- Liver failure (hepatic failure)
- Infertility in males
- Severe infection throughout the body (sepsis)

Obinutuzumab (GAZYVA®)

Likely:

- Low white blood cell count (cells that help fight infection) (neutropenia)
- Low platelet count (cells that help blood to clot) (thrombocytopenia)
- Low red blood cell count (anemia)
- Low white blood cell counts with fever (febrile neutropenia)
- Fatigue
- Infusion reactions (see additional information below)
- Fever (pyrexia)
- Nausea
- Vomiting
- Diarrhea
- Constipation
- Decreased appetite
- Cough
- Infections, the most common include: upper respiratory tract infection, sinusitis, urinary tract infection
- General weakness (asthenia)
- Joint or muscle pain (arthralgia or musculoskeletal pain)

Less Likely:

- Low number of other white blood cells, cells that help fight infection; with or without fever (including granulocytopenia, leukopenia, lymphopenia)
- Heartburn or indigestion (dyspepsia)
- Sore throat (nasopharyngitis, pharyngitis)
- Joint aches (arthralgia)
- Pain in extremity
- Nasal congestion
- Itching (pruritus)
- Chemical imbalance in blood (including low albumin calcium, phosphate, potassium and sodium, and high levels of liver enzymes)
- Abnormal blood clotting (Disseminated Intravascular Coagulation)
- Intestinal perforation
- Basal Cell Carcinoma
- Squamous Cell Carcinoma
- Cytokine Release Syndrome

Rare but Serious:

- Effects on the heart (see additional information below)

More information:

Allergic and infusion reactions: Sometimes people have allergic reactions to drugs. Serious allergic reactions can be life-threatening. If you have an allergic reaction, you might develop a rash, difficulty breathing, wheezing when you breathe, sudden low blood pressure with light-headedness, swelling around the mouth, throat or eyes, a racing heartbeat, and/or sweating. Before starting the study drug, you must tell your study doctor about any drug allergies. You should tell a member of the study team right away if you have any allergy symptoms listed above.

Bleeding effects: You may experience bruising or nose bleeds during dosing. Rarely, serious internal bleeding, such as bleeding in your stomach, intestine, or brain may occur sometimes resulting in death. If you take medicines or supplements that increase your risk of bleeding, such as aspirin, non-steroidal anti-inflammatory drugs (NSAIDs) or medicines used to prevent or treat blood clots or stroke, some medications, including ibrutinib and obinutuzumab, may increase this risk. Blood thinners such as warfarin or other vitamin K antagonists should not be taken together with ibrutinib and obinutuzumab. If you have signs or symptoms of severe bleeding in or around the brain (such as sudden severe headaches, weakness in the arms or legs, difficulty speaking or understanding speech, or loss of balance) or if you have signs or symptoms of serious bleeding (such as blood in your stools or urine or bleeding that lasts for a long time or that you cannot control), please call the study team right away.

Effects on the heart: Abnormal heartbeats (atrial fibrillation and/or atrial flutter) and worsening of heart conditions have been reported in patients treated with ibrutinib and obinutuzumab, especially when they also have a history of these and other heart conditions, including increased blood pressure, infections, or had abnormal heartbeat in the past. Atrial fibrillation/flutter is a common type of abnormal heartbeat. The heartbeat may be fast or irregular causing symptoms such as a pounding or racing heart, dizziness, weakness, feeling light-headed or shortness of breath. If you develop any of these symptoms while on the study drug, you should tell your study doctor immediately.

Hepatitis B Reactivation: In patients with a history of hepatitis B infection, taking obinutuzumab could cause it to return. You should not receive obinutuzumab or any of the study medications if you have active hepatitis B or C liver disease. We will screen you at baseline for hepatitis and monitor you during the study. You should tell your study doctor immediately if you have any of these symptoms which may suggest hepatitis: worsening of fatigue and yellow discoloration of the skin or eyes.

Infection:

- A rare and usually fatal viral disease in the brain, Progressive Multifocal Leukoencephalopathy (PML), has been reported in patients treated with obinutuzumab. If you experience symptoms such as weakness, paralysis, vision loss and/or impaired speech, you should tell the study team immediately.
- Patients with MZL who receive obinutuzimab are at a higher risk for developing a fungal infection of the lungs that can cause pneumonia (Pneumocystis Jiroveci pneumonia). For

this reason, all patients with MZL will receive medication from the start of therapy until completion to prevent this infection.

Magrolimab

The following events have been observed in at least 1 out of 10 patients treated with magrolimab (taken alone or with another anti-cancer drug):

- Red blood cell agglutination (red blood cells sticking together when viewed on a glass slide under the microscope)
- Thrombocytopenia (abnormally low platelets in the blood)
- Nausea
- Diarrhea
- Vomiting
- Constipation
- Abdominal pain
- Fatigue
- Fever
- Chills
- Infusion- related reaction (allergic reaction to drugs while it is being given into your vein or shortly thereafter)
- Blood bilirubin increased (increase of orange-yellow pigment that occurs normally when part of your red blood cells break down)
- Decreased appetite
- Back Pain
- Headache
- Cough
- Shortness of breath
- Dizziness (lightheadedness)
- Joint aches (arthralgia)
- Low white blood cell counts with fever (febrile neutropenia)
- Low white blood cell count (cells that help fight infection) (neutropenia)
- Difficulty breathing (dyspnea)

- Hypophosphatemia (low phosphorus in your blood)
- Hypokalemia (decrease of potassium in the blood)
- Hypotension (low blood pressure)
- Peripheral edema (swelling and fluid retention in the arms and legs)
- Pneumonia (lung infection)
- Pruritus (itchy skin)
- Severe infection throughout the body (sepsis)
- Anemia (abnormally low number of red blood cells) and hemolysis (destruction of red blood cells): The study drug, magrolimab, attaches to red blood cells. When it attaches to old red blood cells, some of the old red blood cells may die, causing anemia, especially at the beginning of the treatment. Anemia is detected by a blood test counting the red blood cells, and can cause pale skin, fatigue and loss of energy, shortness of breath, low blood pressure and/or rapid heartbeats. In a few patients treated with magrolimab, anemia or the effects of anemia have been life-threatening or fatal. Sudden deaths have occurred during or shortly after initial treatment doses. Your study doctor will test your blood for anemia before each magrolimab infusion during the study, and a few hours after you start the first and second doses of magrolimab. Your blood may also be tested more often if your study doctor is concerned about anemia. If anemia is severe, your doctor may recommend a blood transfusion to increase the number of your red blood cells and/or stop or delay treatment altogether with magrolimab. It is important that you inform the study doctor about any past known or suspected cardiovascular (heart) disease and any related symptoms, including but not limited to: chest pain, difficulty breathing, and swelling of the lower limbs before participating in the study. These conditions may increase your risk of side effects from anemia.
- Pneumonitis and respiratory distress: Cases of lung inflammation (pneumonitis) and respiratory distress have been reported with magrolimab use. All reported patients were also receiving other medications that are known to cause lung toxicity and respiratory distress. Common symptoms of pneumonitis are cough and shortness of breath. Pneumonitis is diagnosed by imaging (chest X-ray or CT scan). If detected, your study doctor may delay, or stop treatment with magrolimab. Your study doctor may also give you oxygen and some drugs to treat the symptoms. In some cases, hospitalization may be required. For your safety, the study doctor will monitor you for these events. For example, respiratory rate and oxygen saturation will be checked at every follow-up visit. You will be asked for respiratory symptoms during follow-up visits as well. Patients with known lung and heart conditions will be monitored closely.
- Infusion Reactions: Magrolimab may cause side effects similar to an allergic reaction, called an infusion reaction, while it is being given into your vein or shortly after it is given, especially during/after the 2 first doses. These reactions could include symptoms such as fever, chills, back pain, nausea, vomiting, and shortness of breath. To-date, these reactions were observed to be mild to severe. Before each administration of the first 2 doses of magrolimab, you will receive medications in an attempt to minimize the risk of occurrence

of infusion reaction. If you experience these symptoms, your study doctor may slow down, interrupt, or even stop the delivery of magrolimab into your vein. Your study doctor may also give you some drugs to treat these symptoms. In some cases, you might be admitted to the hospital for treatment and monitoring. You will receive medications before your initial treatments of magrolimab in an attempt to minimize the risk of occurrence of these signs/symptoms. If you have experienced infusion reactions, your study doctor may prescribe premedication prior to your next treatment with magrolimab or discontinue treatment with magrolimab permanently. For your safety, the study doctor will monitor you for these events. For example, you will have your blood pressure, pulse, body temperature, and respiratory rate monitored before and for 1 hour after the magrolimab infusions for the first four weeks. If you are receiving magrolimab and experience a reaction that could be related to magrolimab, we may stop the infusion, and you may be withdrawn from the study if the reaction is severe or it recurs.

- Hemagglutination: Studies in test tubes have shown that the study drug can make the red blood cells sticky – this is known as hemagglutination. This may be a potential concern because sticky red blood cells can cause tiny clots, which may obstruct normal blood flow in the smallest blood vessels and cause ischemia (restriction of blood and oxygen supply to tissues), including blood vessels in the eyes. Patients treated with magrolimab have been found to have clumping of red blood cells on a glass slide under the microscope; however, most of these patients did not have side effects that could be directly linked to that observation. In earlier studies, the sponsor checked blood smears and performed vision tests during each treatment cycle and did not observe clinically significant hemagglutination. These tests will continue to be done as part of this study.
- Anti-drug Antibody Reactions: In some patients, treatment with magrolimab causes the body's immune system to develop special antibodies directed at magrolimab. These antibodies can affect how magrolimab is handled by your body. Antibodies are proteins made in the body that respond to a substance that is foreign to the body. If you develop these special antibodies, it may affect your body's ability to respond to magrolimab in the future and might produce side effects including infusion reactions or problems with your kidneys. Blood samples will be drawn to monitor for the development of these antibodies during study treatment and 30 days after your last infusion of study drug.
- Other Laboratory Abnormalities: Thrombocytopenia (abnormally low platelets in the blood) was observed in at least 1 out of 10 patients treated with magrolimab. Platelets are colorless blood cells that help blood to clot. Low platelets could lead to bleeding. If your platelets go too low, your doctor may prescribe appropriate treatment. Other laboratory abnormalities experienced by at least one out of 10 patients included low neutrophils which can lead to increased risk of infection, hyperbilirubinemia (increase of orange-yellow pigment that occurs normally when part of your red blood cells break down, also known as jaundice) and hypokalemia (decrease of potassium in the blood).

- Thromboembolic events: Blood clots forming in blood vessels such as large veins or arteries have been reported in some patients receiving magrolimab, sometimes early in therapy. These clots have mostly been found in the lung arteries and in deep veins. Clots

in the lung arteries can lead to difficulty breathing and heart issues. Clots in the leg deep veins can cause leg swelling and pain. It is currently unknown if magrolimab increases your risk of getting blood clots. Your study doctor will monitor you carefully for potential clots and take proper medical action including possibly having you take anti-clotting medications if any such situations arise. Please contact your doctor immediately if you experience shortness of breath, weakness or chest pain.

- Interactions with Other Drugs: magrolimab may have some side effects that may overlap with some of the side effects caused by other medications that also stimulate the immune system. It may be dangerous to take both/all of these drugs at the same time. It is important to inform your doctor the last time you took any medication or nutritional supplements that stimulate the immune system. Your study doctor will discuss this with you further.
- Risks Related to Blood Type and Cross-Match Testing: Based on studies in the laboratory using human blood samples, magrolimab may interfere with some of the tests used to determine your blood type. This may require that special additional testing be performed on your blood if you were to need a blood transfusion for any reason. For any non-emergency blood transfusion, you will be required to go to a site, or come back to our clinic, where the appropriate testing can be performed. In the event of an emergency and you are taken to another hospital, the emergency doctors should contact the magrolimab study doctor immediately. The primary risk of interference of the blood type and cross match results is that you could receive blood that is the wrong type, resulting in a serious and life-threatening reaction or death.

Other General Risks

Tumor Lysis Syndrome: You may experience a large release of tumor cell chemicals in the blood after treatment, which could lead to kidney failure and possibly death. This may lead to changes in kidney function, abnormal heartbeat, or seizures. Your study doctor may do blood tests to check for TLS, and treat you for it as needed. This may include possible inpatient admission in the hospital.

Risks from tests and procedures

The risks of taking part may include the following:

- Blood draws:
    - Likely: discomfort, swelling, bruising, and/or bleeding at the site of the needle insertion.
    - Less likely: dizziness or feeling faint.
    - Rare: infection (symptoms may include fever, shaking, chills, fatigue, confusion, joint aches, or rapid pulse).

  Up to about 7 tablespoons of blood may be collected at any day, up to about 27 tablespoons may be collected within 8 weeks.

- Bone marrow testing: A numbing agent that can cause a stinging or burning sensation may be injected at the site of your bone marrow biopsy. The biopsy needle will go through the

skin into the bone and may produce a brief, sharp pain. As the bone marrow liquid is taken from the bone, there may be a brief, sharp pain. Since the inside of the bone cannot be numbed, this procedure may cause some discomfort, however not all people experience discomfort. The possible side effects associated with a bone marrow biopsy include pain, bleeding, bruising, and infection, as well as a reaction to the numbing agent.

- Biopsy:
  - Likely: discomfort or pain, redness, swelling, and/or bruising at the site of the needle insertion.
  - Less likely: Bleeding from the site of the needle insertion
  - Rare: significant infection or bleeding from this procedure, allergic reaction to the local anesthetic, or formation of a scar at the site of needle entry.

  You will be asked to sign a separate consent form prior to any biopsy procedure.

- Conscious Sedation: The common side effects of conscious sedation include drowsiness, delayed reflexes, hypotension, headache, and nausea. These are generally mild and last no more than a few hours. You will be monitored throughout the procedure.

- Imaging: The following may be done as directed by your doctor based on your disease:
  - CT Scan (computerized tomography): There is a slight risk of developing an allergic reaction to the iodine contrast material. The reaction can be mild (itching, rash) or severe (difficulty breathing or sudden shock). Death resulting from an allergic reaction in this setting is rare. Most reactions can be controlled using drugs. Be sure to tell your doctor if you have allergies of any kind (such as hay fever, iodine allergy, eczema, hives, or food allergies).

    The contrast material used during CT scanning can cause water loss or damage to the kidneys that may lead to kidney failure. This is a concern if you have poor kidney function, dehydration, or diabetes, especially if you take Metformin® (Glucophage) to control diabetes.

    You may also experience discomfort related to lying still in an enclosed space for a prolonged period of time.
  - MRI Risks: MRI uses a strong magnetic field and radio waves to take pictures of the body. We may obtain pictures of your brain or other parts of your body for this study. The MRI scanner is a metal cylinder surrounded by a strong magnetic field. During the MRI, you will lie on a table that can slide in and out of the cylinder. We will place soft padding or a coil around your head. You will be in the scanner about 45 minutes. You may be asked to lie still for up to 15 minutes at a time. While in the scanner you will hear loud knocking noises, and you will be fitted with earplugs or earmuffs to muffle the sound. You will be able to communicate with the MRI staff at all times during your scan, and you may ask to be moved out of the machine at anytime.

It is very important for the experiment that you do not move your head or body inside the scanner. We will use padding around your head to help keep it in place.

We may place a bar in your mouth to help keep your head still.

People are at risk for injury from the MRI magnet if they have some kinds of metal in their body. It may be unsafe for you to have an MRI scan if you have pacemakers or other implanted electrical devices, brain stimulators, some types of dental implants, aneurysm clips (metal clips on the wall of a large artery), metal prostheses (including metal pins and rods, heart valves, and cochlear implants), permanent eyeliner, tattoos, an implanted delivery pump, or shrapnel fragments. Welders and metal workers may have small metal fragments in the eye. You will be screened for these conditions before having any MRI scan. If you have a question about metal in your body, you should inform the staff. You will be asked to complete an MRI screening form before each MRI scan you have.

In addition, all magnetic objects (like watches, coins, jewelry, and credit cards) must be removed before entering the MRI scan room.

People with fear of confined spaces may become anxious during an MRI. Those with back problems may have back pain or discomfort from lying in the scanner. The noise from the scanner is loud enough to damage hearing, especially in people who already have hearing loss. Everyone having a research MRI scan will be fitted with hearing protection. If the hearing protection comes loose during the scan, you should let us know right away.

There are no known long-term risks of MRI scans.

Risks for gadolinium enhanced MRI scans:

Procedure: During part of the MRI you may receive gadolinium, a contrast agent, through an intravenous (IV) catheter. It will be done for medical purposes.

It is not known if MRI with contrast is completely safe for a developing fetus. Therefore, all women of childbearing potential will have a pregnancy test performed no more than 24 hours before each MRI scan with contrast. The scan will not be done if the pregnancy test is positive.

Risks: The risks of an IV catheter include bleeding, infection, or inflammation of the skin and vein with pain and swelling.

Mild symptoms from gadolinium infusion occur in fewer than 1% of those who receive it and usually go away quickly. Mild symptoms may include coldness in the arm during the injection, a metallic taste, headache, and nausea. In an extremely small number, fewer than one in 300,000 people, more severe symptoms have been reported including shortness of breath, wheezing, hives, and lowering of blood pressure. You should not receive gadolinium if you previously had an allergic reaction to it. You will be asked about such allergic reactions before gadolinium is given.

People with kidney disease are at risk for a serious reaction to gadolinium contrast called "nephrogenic systemic fibrosis" which has resulted in a very small number of deaths. A blood test of your kidney function may be done within the month before an MRI scan with gadolinium contrast. You will not receive gadolinium for a research MRI scan if your kidney function is not normal or if you received gadolinium within the previous month.

Most of the gadolinium contrast leaves the body in the urine. However, the FDA has issued a safety alert that indicates small amounts of gadolinium may remain in the body for months to years. The effects of the retained gadolinium are not clear. At this time, retained gadolinium has not been linked to health risks in people whose kidneys work well.

Some types of gadolinium contrast drugs are less likely to remain in the body than others. In this study, we will use the gadolinium contrast drugs that are less likely to remain in the body.

Please tell your research team if you have had any MRI scans in the past 12 months. We will also give you additional information called a "Medication Guide." Upon request, we will give you individual information about retained gadolinium we see on your studies.

What are the risks related to pregnancy?

If you are capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study. You will need to practice an effective form of birth control before starting study treatment, during study treatment, and for 90 days after the last dose of magrolimab, 30 days after the last dose of venetoclax, and 18 months after the last dose of obinutuzumab for women and 6 months after the last dose of obinutuzumab for men, whichever is later (the restricted period). If you become pregnant, there may be unknown risks to the fetus or unborn child, or risks that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to a fetus. You must tell the study doctor if your birth control method fails during the restricted period. If you think or know you have become pregnant during the restricted period, please contact the research team member identified at the top of this document as soon as possible.

If you are a sexually active person with a partner capable of becoming pregnant, it is important that your partner not become pregnant during the restricted period. There may be unknown risks to a fetus or risks we did not anticipate. You and your partner must agree to use birth control if you want to take part in this study. If you think your partner has become pregnant during the restricted period, please contact the research team member identified at the top of this document as soon as possible. If you and your partner plan for your partner to become pregnant after the restricted period, please discuss this with the study team.

What are the risks of radiation from being in the study?

During your participation in this research study, you will be exposed to radiation from CT scans of the chest, abdomen and pelvis, ^{18}F-FDG PET/CTs of the torso and the extremities, and CT-guided biopsies (including screening and treatment). The amount of radiation exposure you will

receive from these procedures is equal to approximately 14.1 rem. A rem is a unit of absorbed radiation. Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. The average person in the United States receives a radiation exposure of 0.3 rem per year from these sources. This type of radiation is called "background radiation." This study will expose you to more radiation than you get from everyday background radiation. No one knows for sure whether exposure to these low amounts of radiation is harmful to your body. The CT scans, ^{18}F-FDG PET/CT, and CT-guided biopsies, that you get in this study will expose you to roughly the same amount of radiation as 35.7 years' worth of background radiation. Being exposed to too much radiation can cause harmful side effects such as an increase in the risk of cancer. The risk depends on how much radiation you are exposed to. Please be aware that about 40 out of 100 people (40%) will get cancer during their lifetime, and 20 out of 100 (20%) will die from cancer. The risk of getting cancer from the radiation exposure in this study is 1.1 out of 100 (1.1%) and of getting a fatal cancer is 0.5 out of 100 (0.5%).

You may not participate in this study if you are pregnant. If you are able to become pregnant, we will perform a pregnancy test before exposing you to radiation. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time.

Psychological or Social Risks Associated with Loss of Privacy

As part of the research study, it is possible that you could learn that you have genetic risks for another disease or disability. This may be upsetting and, depending on what you learn, might create a need to make challenging decisions about how to respond.

Although your genomic information is unique to you, you share some genomic similarities with your children, parents, brothers, sisters, and other blood relatives. Therefore, learning your research results could mean something about your family members and might cause you or your family distress. Before joining the study, it may be beneficial to talk with your family members about whether and how they want you to share your results with them.

Privacy Risks Associated with Return of Incidental or Secondary Findings

As part of the research study, it is possible that you could learn that you have genetic risks for another disease or disability. This may be upsetting and, depending on what you learn, might create a need to make challenging decisions about how to respond.

Although your genomic information is unique to you, you share some genomic similarities with your children, parents, brothers, sisters, and other blood relatives. Therefore, learning your research results could mean something about your family members and might cause you or your family distress. Before joining the study, it may be beneficial to talk with your family members about whether and how they want you to share your results with them.

Protections against misuse of genetic information

This study involves genetic testing on samples. Some genetic information can help predict future health problems of you and your family and this information might be of interest to your employers or insurers. The Genetic Information Nondiscrimination Act (GINA) is a federal law that prohibits plans and health insurers from requesting genetic information or using genetic information. It also prohibits employment discrimination based on your health information. However, GINA does not

address discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed condition or disease that has a genetic component.

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You might not benefit from being in this study.

However, the potential benefit to you might be the shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer.

Are there any potential benefits to others that might result from the study?

In the future, other people might benefit from this study because of the knowledge gained from the study drug combination or the results of the research studies.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

Before you decide whether or not to be in this study, we will discuss other options that are available to you. Instead of being in this study, you could:

- choose to be treated with surgery, radiation or with drugs already approved by the FDA for your disease
- choose to take part in a different study, if one is available
- choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms.

You should discuss with your doctor your other choices and their risks and benefits.

DISCUSSION OF FINDINGS

New information about the study

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have learned while doing this study here at the NIH or information we have learned from other scientists doing similar research in other places.

Return of research results

When we are examining your DNA, it is possible that we could identify possible changes in other parts of your DNA that are not related to this research. These are known as “incidental medical findings”.

These include:

- Changes in genes that are related to diseases other than cancer
- Changes in genes that are not known to cause any disease. These are known as normal variations.
- Changes in genes that are new and of uncertain clinical importance. This means that we do not know if they could cause or contribute to a disease or if they are normal variations.

Since the analyses that we perform in our laboratory are not nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing, the genetic changes that we find may or may not be valid. Therefore, we do not plan to inform you of all of the genetic results of testing on your tissue and blood that is performed in our research lab. However, in the unlikely event that we discover a finding believed to be clinically important based on medical standards at the time we first analyze your results, we will contact you. This could be many years in the future. We will ask you to provide another sample to verify the findings we have seen in our lab. If the results are verified, you will be re-contacted and offered a referral to a genetic Healthcare Provider to discuss the results.

EARLY WITHDRAWAL FROM THE STUDY

Your doctor may decide to stop your therapy for the following reasons:

- if he/she believes that it is in your best interest
- if your disease worsens or comes back during treatment
- if you have side effects from the treatment that your doctor thinks are too severe
- if you become pregnant
- if the study drugs may become unavailable
- if new information shows that another treatment would be better for you
- if you do not follow the study rules
- if the study is stopped for any reason

In this case, you will be informed of the reason therapy is being stopped.

After therapy is stopped we would like to see you for a safety visit 30 days after your last dose.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to the Gilead Sciences Inc., AbbVie, Inc., Genentech, Inc., or designated representatives.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

Will your specimens or data be saved for use in other research studies?

As part of this study, we are obtaining specimens and data from you. We will remove all the identifiers, such as your name, date of birth, address, or medical record number and label your specimens and data with a code so that you cannot easily be identified. However, the code will be linked through a key to information that can identify you. We plan to store and use these specimens and data for studies other than the ones described in this consent form that are going on right now, as well as studies that may be conducted in the future. These studies may provide additional information that will be helpful in understanding lymphoma, or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to the development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this

happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you.

I give permission for my coded specimens and data to be stored and used for future research as described above.

_____ Yes _____ No

Initials Initials

Will your specimens or data be shared for use in other research studies?

We may share your coded specimens and data with other researchers. If we do, while we will maintain the code key, we will not share it, so the other researchers will not be able to identify you. They may be doing research in areas that are similar to this study or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or commercial entities.

I give permission for my coded specimens and data to be shared with other researchers and used by these researchers for future research as described above.

_____ Yes _____ No

Initials Initials

If you change your mind and do not want us to store and use your specimens and data for future research, you should contact the research team member identified at the top of this document. We will do our best to comply with your request but cannot guarantee that we will always be able to destroy your specimens and data. For example, if some research with your specimens and data has already been completed, the information from that research may still be used. Also, for example, if the specimens and data have been shared already with other researchers, it might not be possible to withdraw them.

In addition to the planned use and sharing described above, we might remove all identifiers and codes from your specimens and data and use or share them with other researchers for future research at the NIH or other places. When we or the other researchers access your anonymized data, there will be no way to link the specimens or data back to you. We will not contact you to ask your permission or otherwise inform you before we do this. We might do this even if you answered "no" to the above questions. If we do this, we would not be able to remove your specimens or data to prevent their use in future research studies, even if you asked, because we will not be able to tell which are your specimens or data.

NIH policies require that your clinical and other study data be placed in an internal NIH database that is accessible to other NIH researchers for future research. Usually, these researchers will not have access to any of your identifiers, such as your name, date of birth, address, or medical

record number; and your data will be labeled with only a code. We cannot offer you a choice of whether your data to be placed in this database or not. If you do not wish to have your data placed in this database, you should not enroll in this study.

Will your genomic data be shared outside of this study?

As part of this research study, we will put your genomic data in a large database for broad sharing with the research community. These databases are commonly called data repositories. The information in this database will include but is not limited to genetic information, race and ethnicity, and sex. If your individual data are placed in one of these repositories, they will be labeled with a code and not with your name or other information that could be used to easily identify you, and only qualified researchers will be able to access them. These researchers must receive prior approval from individuals or committees with authority to determine whether these researchers can access the data.

Summary information about all of the participants included in this study (including you) is being placed in a database and will be available through open access. That means that researchers and non-researchers will be able to access summary information about all the participants included in the study, or summary information combined from multiple studies, without applying for permission. The risk of anyone identifying you with this information is very low.

in a repository for sharing. Therefore, we cannot offer you a choice of whether your data will be shared. If you do not wish to have your data placed in a repository, you should not enroll in this study.

How long will your specimens and data be stored by the NIH?

Your specimens and data may be stored by the NIH for as long as the study is open. When this study is closed, we will keep the samples for future research indefinitely.

Risks of storage and sharing of specimens and data

When we store your specimens and data, we take precautions to protect your information from others that should not have access to it. When we share your specimens and data, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your specimens and data.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. The amount and form of these payments are determined by the NCI Travel and Lodging Reimbursement Policy. You will be given a summary of the policy which provides more information.

If your travel to the NIH Clinical Center (e.g., flight, hotel) is arranged and paid for by the NIH, the agency making the reservations and their representatives will have access to your identifiable information.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center. .

- If some tests and procedures are performed outside the NIH Clinical Center, you may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CONFLICT OF INTEREST (COI)

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a COI Guide. You may ask your research team for a copy of the COI Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines or the guidelines of their home institution, but they do not need to report their personal finances to the NIH.

The following pharmaceutical collaborators are providing the following drugs for this study to NIH without charge:

- Gilead Sciences, Inc. is providing magrolimab
- AbbVie, Inc. manufactures venetoclax
- Genentech, Inc., is providing ventoclax and obinutuzumab

No NIH investigator involved in this study receives payments or other benefits from any company whose drug, product or device is being tested. However, there are some research partners not associated with the NIH working on this study who may receive payments or benefits, limited by the rules of their workplace.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you.

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- Qualified representatives from Gilead Sciences, Inc., the pharmaceutical company who provides magrolimab.
- Qualified representatives from AbbVie, Inc., the pharmaceutical company who produces venetoclax.
- Qualified representatives from Genentech, Inc., the pharmaceutical company who provides venetoclax and obinutuzumab.

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical information that we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Mark Roschewski, M.D., Building 10, Room 4N115, Telephone: 240-760-6183. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness should sign below if either:

1. **A short form consent process has been used to enroll a non-English speaking subject or**
2. **An oral presentation of the full consent has been used to enroll a blind or illiterate subject**

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____